A Web-Service Approach for Distributed Access to Methods, Data and Models

(I Don't Care Where My Data and Methods Are)

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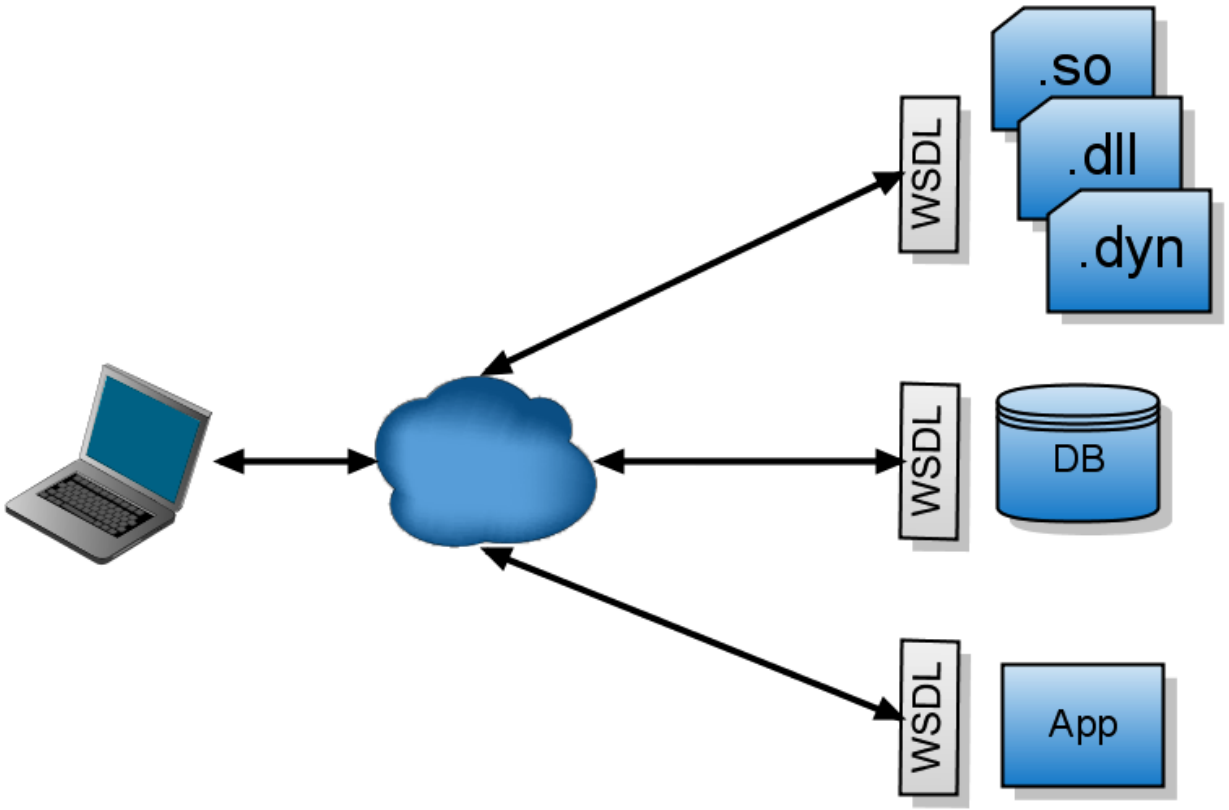
Outline

Local versus Distributed Resources



- Access arbitrary resources (methods, data, applications)
- All resources look like function calls

Combining Data & Functionality

- But what do we mean by "combining" all these resources?
- Different levels of complexity
  - Keep track of new additions to a database via an RSS feed
  - Use Yahoo Pipes to combine and manipulate output easily
  - Write full fledged programs in your language of choice
- Web services allow us to support all these activities in a uniform manner

Web Services - What's Available

Cheminformatics functionality

- Molecular descriptors
- Similarity (2D, 3D)
- Format conversion
- Depictions
- 3D coordinate generation
- Summarized on ChemBioGrid

Dong, X. et al, *J. Chem. Inf. Model.*, **2007**, *47*, 1303–1307

`http://www.chembiogrid.org/projects/proj_core.html`

Web Services for Modeling

- Computational web services can be viewed as wrappers around the actual program
- Since predictive models are a common feature in cheminformatics we'd like to support them as well
- This leads to a number of requirements
  - Ability to develop models
  - Store (deploy) models
  - Use the models via the web service infrastructure
- We provide a computational infrastructure based on R which supports
  - Feature selection
  - Model development
  - Model deployment
  - Arbitrary R code

Guha, R. *J. Chem. Inf. Model.*, **2008**, *48*, 456–464

What's Available?

- Regression (OLS, CNN, RF)
- Classification (LDA)
- Clustering (k-means)
- Feature selection (stepwise and exhaustive)
- Automated model generation
  - Load X, Y data, build linear and non-linear models with optional LOO CV
- Deployed models
  - Random forests for 60 NCI DTP cell lines
  - Cytotoxicity
  - Ames mutagenicity

Wang, H. et al., *J. Chem. Inf. Model.*, **2007**, *47*, 2063–2076

Guha, R. and Schürer, S., *J. Comp. Aid. Molec. Des*, **2008**, ASAP

Web Services - What's Available

Data sources

- We maintain a number of databases
  - PubChem mirror (mainly for local research)
  - Pub3D
- Directly accessible via queries in SQL
- We also encapsulate specific queries as web service calls

http://www.chembiogrid.org/projects/proj_db.html

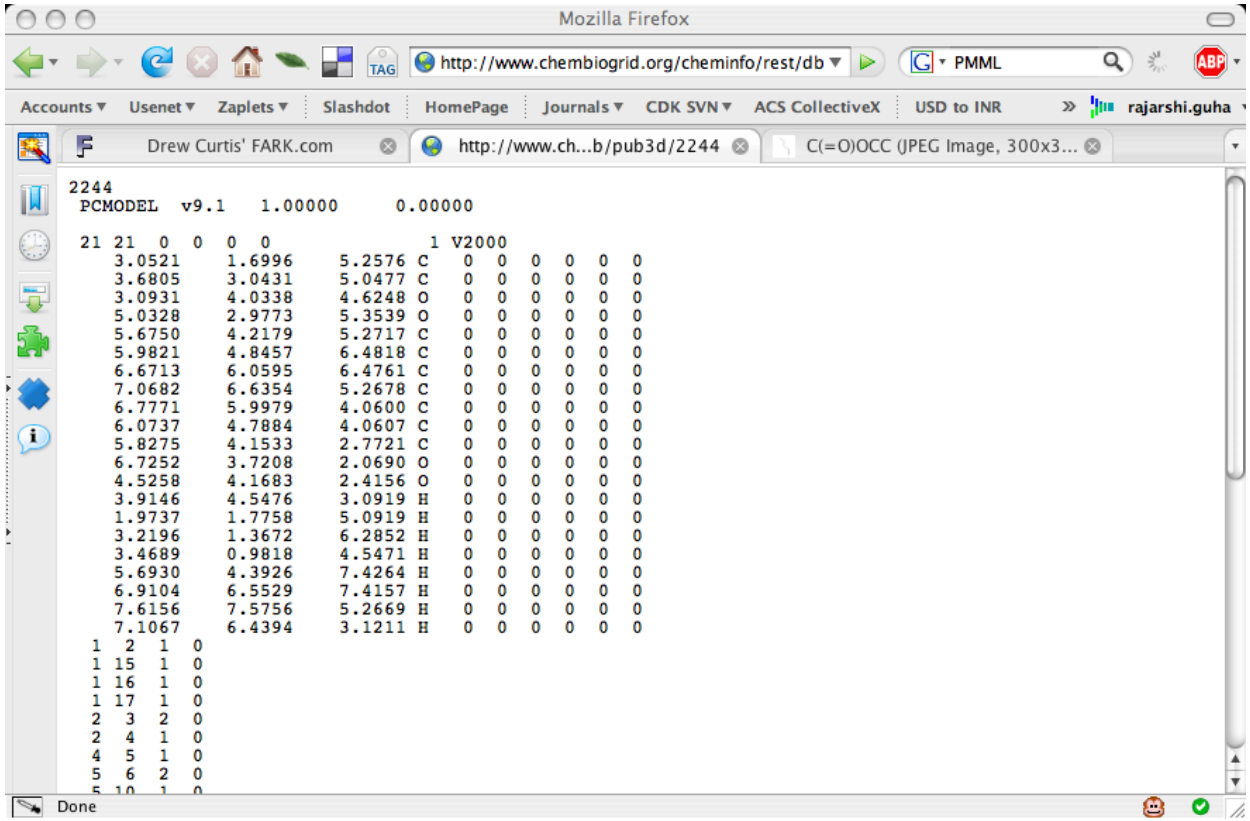
REST Frontends to SOAP Services

- REST is a network architecture that avoids complex message formats
  - No extra libraries required
  - Access services using URL's
  - Much simpler interface compared to SOAP
- We've been putting REST interfaces onto a number of our SOAP services
- Current REST services include
  - Database (3D structure, PubChem mirror)
  - Molecular descriptors
  - Depictions

REST 3D Structure Service

- To get a 3D structure for a PubChem CID

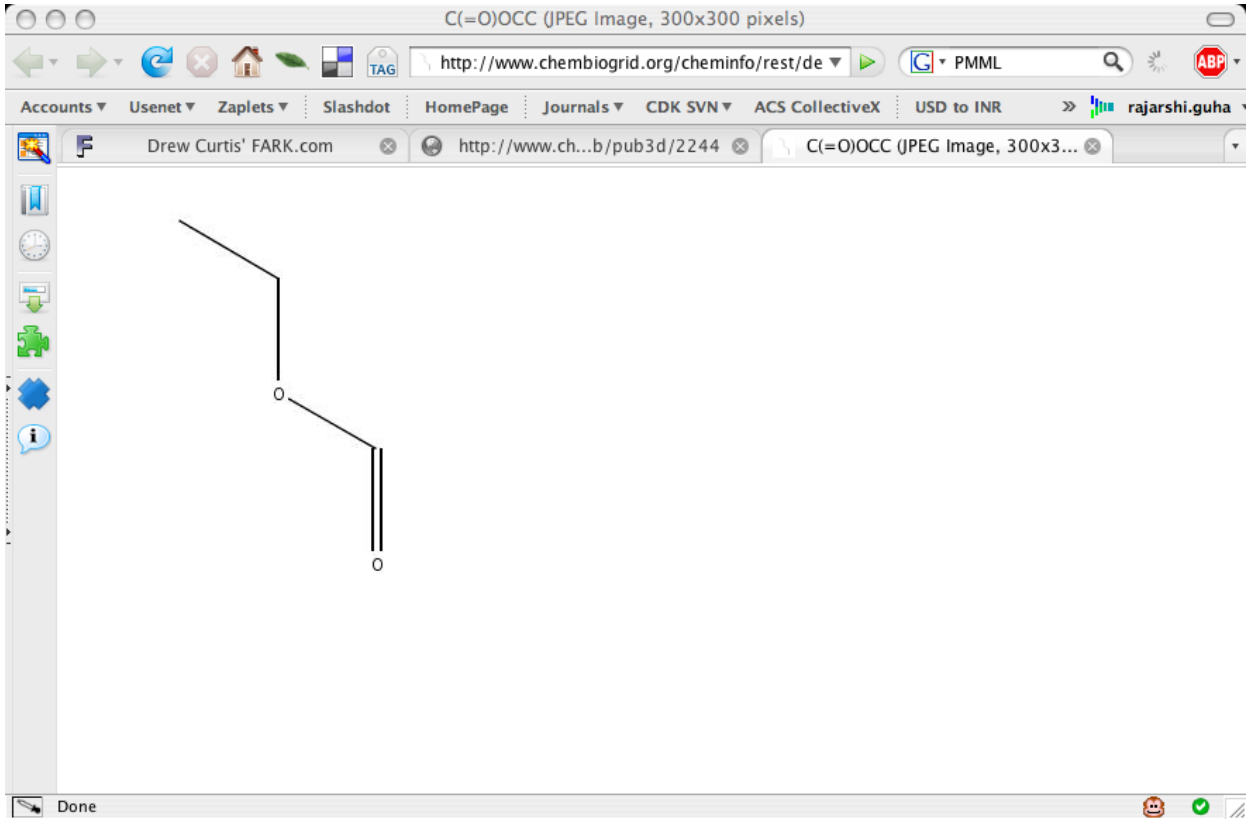
```
http://www.chembiogrid.org/cheminfo/rest/db/pub3d/2244
```



REST Depiction Service

- To get a 2D depiction for arbitrary SMILES

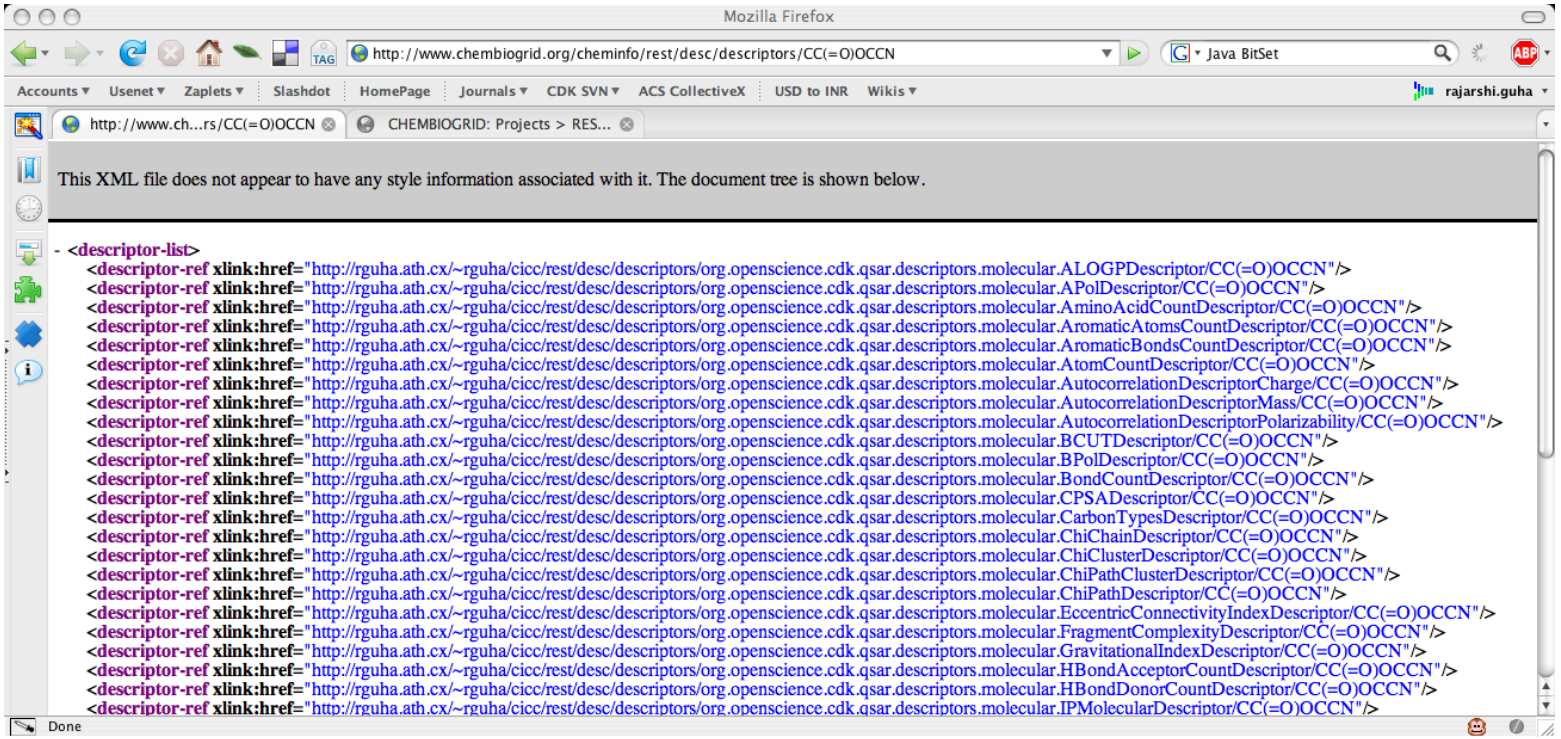
```
http://www.chembiogrid.org/cheminfo/rest/depict/C(=O)OCC
```



REST Descriptor Service

- To get descriptors for an arbitrary SMILES string

```
http://www.chembiogrid.org/cheminfo/rest/desc/
descriptors/CC(=O)OCCN
```



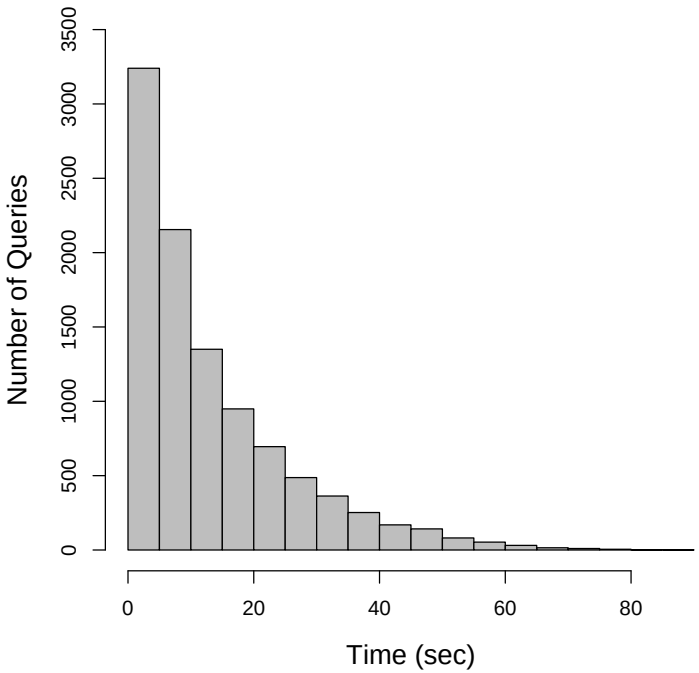
Pub3D

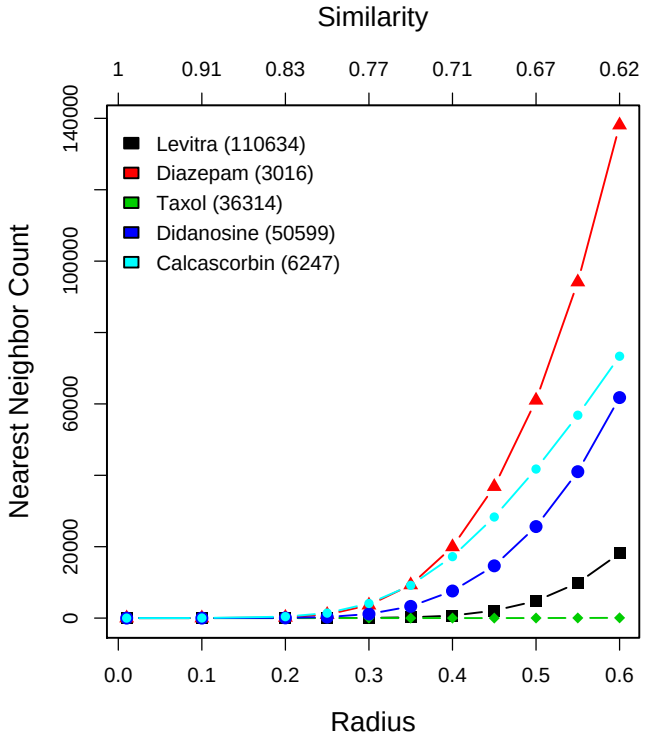
- A 3D structure database derived from PubChem
- Current version contains a single 3D structure for 17M compounds
  - Structures obtained using MMFF94
  - Not the lowest energy conformer
- Structures can be retrieved in SD format by CID using a web page or web service interfaces
- We also store distance moment shape descriptors allowing us to perform shape similarity searches
- http://www.chembiogrid.org/cheminfo/p3d/

Ballester, P.J. and Graham Richards, W., *J. Comp. Chem.*, **2007**, *28*, 1711–1723

Pub3D Performance

- Shape searches can be as fast as 5s, for reasonably large result sets
- Fast enough for us to explore the "density of space" around a given query compound

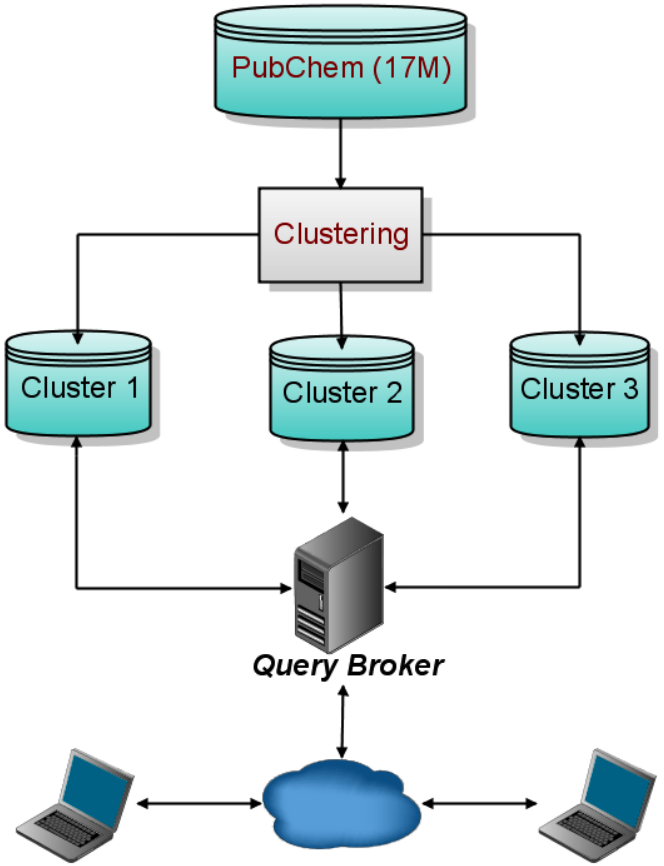




Guha, R. et al., *J. Chem. Inf. Model.*, **2006**, *46*, 1713–1722

Pub3D & Clustering

- Indexing gives good performance
- As index size increases, performance degrades
- Could add more RAM
- Clustering the database allows us to scale to significantly larger collections



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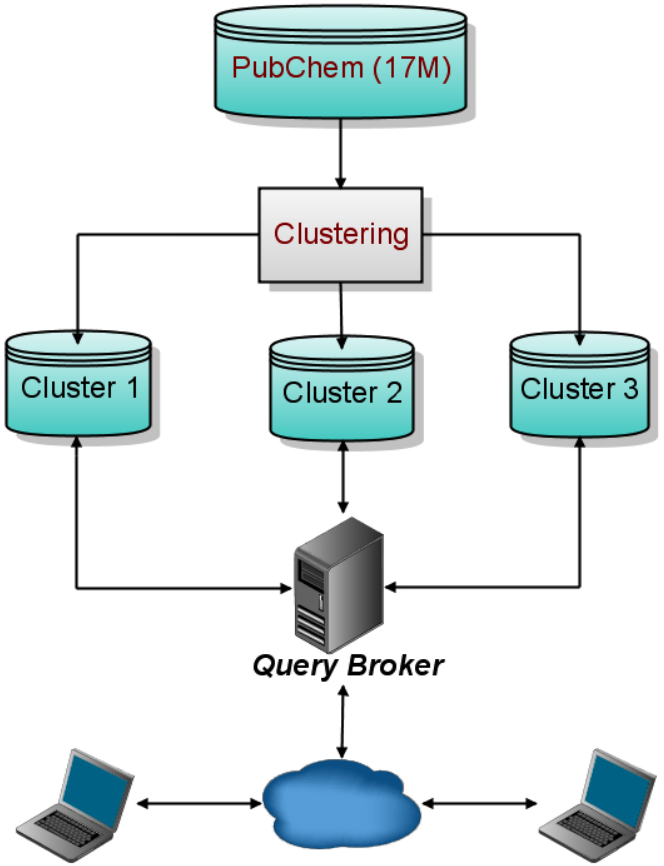

Pub3D and Conformers

- Single, arbitrary conformers aren't too useful
- We have currently generated conformers for a subset of PubChem (4 to 10 heavy atoms)
  - 3 Kcal energy window
  - 243,892 compounds
  - $\approx$ 2M conformers
- Clustering will be vital when conformers are considered
  - Allows us to handle arbitrary numbers of conformers
  - May need to consider some sort of compression
  - Could use cluster information to optimize queries

Model Exchange

- The literature contains many published models
- No way to utilize them unless we manually rebuild them
  - In many cases we will not have access to descriptors
- Difficult to search for models specifically
- We should be able to do the following
  - Search for models
  - Exchange them
  - Execute them
- Is this a "format" issue?
  - To some extent yes

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PMML for Model Exchange

- **P**redictive **M**odelling **M**arkup **L**anguage
- A standard supported by the Data Modeling Group
- Allows you to serialize predictive models to XML
  - Linear, logistic regression
  - Tree models
  - Neural networks, Naïve Bayes models
  - Association models
  - Ensemble models (random forests, arbitrary ensembles)
- Supported by a number of platforms
  - IBM, Salford Systems
  - SAS, SPSS
  - R

PMML for Model Exchange

- Since it's XML, it's extensible
- PMML allows us to specify the model itself
- But we need to add extra information to make a model truly searchable
  - Provenance (who made it, when was it made, . . .)
  - Property (what is being modeled)
  - Requirements (what are the inputs, how to get them)

PMML for Model Exchange

Provenance

- Easily solved using Dublin Core

Property

- Could be addressed using keywords
- Could reuse pre-existing ontologies

Requirements

- This is tricky
- Need to identify what descriptors were used
- What software, version
- How to evaluate the descriptors (if possible)

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Summary

- Pub3D is a shape searchable version of PubChem
- Conformers will have to be considered for it to be useful
- Are searches meaningful? Benchmarks required

- Web services provide one approach to model deployment
- We should be able to search for models explicitly
- PMML is one extensible solution the addresses model exchange
- Automated model execution is more challenging

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Acknowledgments

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